

### **Remarks**

Applicants appreciate the thorough examination of the present application as evidenced by the final Office Action dated December 28, 2004 (hereinafter, the "Final Action"). Claims 16, 22, 31-33 and 41-43 are pending in the present application upon entry of this Amendment. Applicants have amended Claims 16, 31 and 32. Support for the claim amendments can be found throughout the specification, originally filed claims and drawings. Thus, no new matter is believed to be introduced by these claim amendments, and the entry of these amendments is respectfully requested. Applicants further respectfully submit that the present application is in condition for allowance for at least the reasons set forth below.

#### **I. Interview Summary**

Applicants wish to express their appreciation to the Examiner for the courtesy extended to Dr. Sigounas and Applicants' legal representative, Shawna Cannon Lemon, during the in-office interview on August 11, 2005. Applicants further wish to express their appreciation for the considerable time and effort expended by the Examiner during the interview.

During the interview, Dr. Sigounas and the Examiner discussed various aspects of the invention and the cited art.<sup>1</sup> Dr. Sigounas reviewed the background and history of the problem to be solved, *i.e.*, preventing and treating endothelial injury, in particular, endothelial injury caused by chemicals. Dr. Sigounas also discussed the treatment protocols associated with treatment of anemic cancer patients who are administered erythropoietin (EPO) to treat anemia and contrasted this protocol with the current regimen directed to using (EPO) to prevent and/or treat endothelial injury. The Examiner and Dr. Sigounas further discussed several references, presently or previously recited, and their relationship to the present invention.

At the conclusion of the interview, the Examiner requested that evidence showing that the Applicants hypothesized that administration of EPO mitigated the damaging effects on the endothelium caused by a chemotherapeutic agent be provided in the form of a Declaration. The Examiner indicated that he would review the written documents prior to making a final determination. Applicants submit herewith a Declaration Under 37 C.F.R. §

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<sup>1</sup> A portion of the interview was also attended by Examiner Susan NMN Ungar. Dr. Ungar is the Examiner of record for related application U.S. Patent Application Serial No. 09/525,797 (Attorney Docket No. 5218-39B).

1.132 of George Sigounas, Ph.D. (hereinafter, the "Sigounas Declaration") pursuant to the Examiner's request.

## II. Claim Rejections Under 35 U.S.C. §§102 and 103

Claims 16, 17, 19, 20 and 31-33 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Silvestris et al. *Ann Hematol.* 70(6): 313-318 (1995) for reasons previously made of record. Claims 16, 17, 22, 31-33 and 40 stand rejected 35 U.S.C. § 102(b) as being anticipated by JP 02 096535 to Chugai Pharm. Co. Ltd. for reasons previously made of record. Claims 16, 17, 19, 20 and 31-33 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Bukowski et al. *Blood* 84 (10 Supp. 1): 129A (1994) for reasons previously made of record. Claims 16, 17, 19, 20, 22, 31-33 and 40 stand rejected under 35 U.S.C. § 103 as being obvious in view of the combination of the cited references listed above. Applicants respectfully submit that the pending claims are neither anticipated nor obvious in view of the cited references.

As noted in the Sigounas Declaration, Applicants hypothesized that EPO protects and/or repairs endothelial cells and the endothelium from toxicity induced by chemotherapeutic agents. The present specification provides *in vitro* data in support of the ability of EPO to protect and/or repair endothelial cells from toxicity induced by chemotherapeutic agents, and the Sigounas Declaration sets forth the *in vivo* data in support of the same.

None of the cited references teach or suggest the recitations of currently amended independent Claims 16, 31 and 32 and new Claim 43. As noted in the Sigounas Declaration, cancer patients typically receive EPO only after being diagnosed with anemia. Thus, references directed to administration of EPO to anemic cancer patients do not teach or suggest providing an **endothelial-protecting amount of EPO** to patients to protect or repair the endothelium and the these references fail to teach or suggest administering EPO **prior to** receiving chemotherapy. Further, as noted in the Final Action, not all of the cited references teach intravenous administration of EPO. *See* Final Action, page 8. Yet, the Final Action asserts that it would have been *prima facie* obvious to provide intravenous administration of EPO to subjects treated with chemotherapeutics for the purposes of treating endothelial injury. *See* Final Action, page 8. In contrast to the assertions of the Final Action, it would **not** have been obvious to combine these references, at least in view of the distinction that the

references are not directed to the "same population of subjects." As noted above, and further explained in detail in the Sigounas Declaration, anemic cancer patients typically do not receive EPO prior to chemotherapy. Accordingly, prior to the Applicants' discovery, there was no motivation to provide EPO to cancer patients other than to treat anemia and only after initiation of chemotherapy.

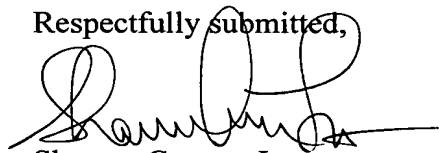
At least in view of the foregoing, Applicants respectfully submit that Claims 16, 22, 31-33 and new Claims 41-43 are patentable, and Applicants respectfully request withdrawal of the claim rejections.

### **Conclusion**

In view of the foregoing amendments and remarks, Applicants respectfully request that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

It is not believed that any fee(s) are required beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that additional fees are necessary to allow consideration of this paper, such an extension is also hereby petitioned for under 37 C.F.R. §1.136(a). Applicants authorize that any additional fees believed to be due in connection with this paper may be charged to Deposit Account No. 50-0220.

Respectfully submitted,



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